isovolumic wall stress decay (τ_c), early LV filling fraction (EFF), and chamber and myocardial stiffness constants (K_c, K_m).

Results: Chronic MR increased diastolic filling volume (FV) by 27% ($P < 0.05$). Chronic MR decreased minimum -dP/dt and increased both τ and τ_c. No statistically significant differences were observed in K_c or K_m (Table). [mean ± SD; *$P < 0.05$; ¶P = N.S. by t-test].

	(-)dP/dt* (mmHg/s)	τ* (ms)	τ_c* (ms)	EFF*	K_c¶	K_m¶
Acute	-1596	39.3	38.9	0.55	0.90	22.2
MR	+279	+4.5	+4.7	+0.21	+0.44	+17.3
Chronic	-1424	45.0	45.6	0.74	0.82	22.5
MR	+308	+8.3	+7.9	+0.22	+0.56	+15.7

Conclusion: Diastolic function is impaired in the progression from acute to chronic MR without changes in myocardial or chamber stiffness properties in this canine model of MR. Diastolic dysfunction in chronic MR is associated with changes in LV filling pattern as evidenced by the increase in EFF.

3:15

852-6 Importance of Mitral Annular Performance in Determining the Mechanism of Functional Mitral Regurgitation

A.U. Chai, C.A. Roldan, M.H. Crawford. *University of New Mexico HSC and Albuquerque VAMC, Albuquerque NM, Mexico*

The mechanism of functional mitral regurgitation (MR) is not well defined. Both an increase in annular diameter and changes in mitral valve apparatus geometry as a result of changes in LV shape have been implicated in the past. Dobutamine stimulation would be expected to change LV systolic function and mitral valve geometry, therefore, comparing the LV shape, and mitral annular diameter at rest and peak dobutamine dose would aid in understanding the mechanism of functional MR. We studied 12 male patients without significant angiographic coronary artery disease with at least mild functional MR. Standard TEE views were obtained at rest and peak dobutamine infusion (25 ± 9 ug/kg/min). Dobutamine decreased LV end systolic volume (LVESV) from 130 ± 55 ml to 103 ± 45 ml ($p < 0.01$) and increased the LV ejection fraction (EF) from 20 ± 10% to 31 ± 12% ($p < 0.01$) and significantly decreased the MR jet area from 3.1 ± 1.6 cm^2 to 1.0 ± 1.5 cm^2 ($p < 0.001$). However, the changes in LVESV and EF did not correlate with the reduction in MR severity ($r = 0.39$ and -0.28, respectively). Dobutamine also significantly decreased the mitral annular diameter in systole (3.9 ± 0.3 cm to 3.6 ± 0.3 cm; $p < 0.01$) and in diastole (4.1 ± 0.3 cm to 3.8 ± 0.3 cm, $p < 0.02$). Mitral annular shortening and shortening fraction also improved with dobutamine and correlated well with changes in MR severity ($r = 0.80$, $p < 0.01$ and $r = 0.79$, $p < 0.01$). We conclude that functional mitral regurgitation appears to be more closely related to changes in annular diameter and contractile state than changes in LV systolic shape or function. Therefore, in patients with significant functional MR, therapeutic attempts at altering LV size or function may be less effective than changing the size of the mitral annulus with an annuloplasty.

853 Transplant Vasculopathy: Clinical Studies

Tuesday, March 31, 1998, 2:00 p.m.–3:30 p.m.
Georgia World Congress Center, Room 254W

2:00

853-1 Development and Progression of Transplant Vasculopathy: Serial Intravascular Ultrasound Study

S.R. Kapadia, K.M. Ziada, T.D. Crowe, J.B. Young, R.C. Starling, M.J. Silver, S.E. Nissen, E.M. Tuzcu. *The Cleveland Clinic Foundation, Cleveland, Ohio, USA*

Background: Although transplant vasculopathy is a major factor limiting outcome after cardiac transplantation, new lesion formation and disease progression over time have not been thoroughly described.

Method: Serial ultrasound was performed 4 weeks, 1 year and 2 years after transplantation (mean 28 ± 17, 370 ± 31, and 761 ± 49 days, respectively). At a series of matched sites, maximum intimal thickness (Pmax) and intimal area were measured at all three time points. Intimal area was defined as the difference between external elastic lamina and lumen areas. A new transplant vasculopathy lesion was defined as Pmax >0.5 mm on follow-up examination at a previously normal site. The availability of 4 week ultrasound measurements enabled exclusion of sites containing donor-transmitted atherosclerosis.

Results: A total of 289 sites in 50 patients were analyzed at all three time points. At one year, 54 sites in 22 patients showed new lesions with Pmax and intimal area averaging 0.76 ± 0.19 mm and 5.60 ± 1.92 mm^2, respectively. At two year follow-up, these same sites showed minimal, if any, progression with Pmax and intimal area averaging 0.78 ± 0.26 mm and 6.14 ± 2.29 mm^2, respectively, p = NS. However, completely new lesions developed at 52 sites in 28 patients at two year examination. Of the 28 patients with new disease at two years, 14 did not have any transplant vasculopathy lesions at one year. The severity of late developing lesions was similar to lesions that developed within the first year. Pmax and intimal area averaged 0.77 ± 0.36 mm and 4.83 ± 2.54 mm^2, p = NS compared to the first year lesions.

Conclusion: Transplant vasculopathy is a process characterized by continuous and relatively constant development of new lesions at previously uninvolved sites during the first two years. Typically, progression of existing lesions is very slow with barely detectable changes between the first and second years. Thus, therapy targeted at preventing new lesion formation may significantly improve outcome.

2:15

853-2 Discrepancies Between Morphologic and Functional Changes in Cardiac Allograft Vasculopathy. Assessment by Serial Intracoronary Ultrasound and Doppler Studies

V. Klauss, C. Spes, K.-H. Henneke, J. Rieber, A. Körperg, H. Sinzker, E. Regar, F. Werner, J. Metz, C. Weber, P. Uberfuhr[1], K. Theisen, B. Reichart[1]. *Harald Mudra. Dpt. of Cardiology, Klinikum Innenstadt, Germany; [1]Dpt. of Cardiac Surgery University of Munich, Germany*

Background: Intracoronary ultrasound (IVUS) has the potential to assess the progression of intimal proliferation in transplant coronary artery disease (TxCAD). The functional significance of TxCAD can be determined invasively by measurement of coronary flow reserve (CFR). We sought to evaluate whether a progression of TxCAD is paralleled by an impairment of CFR by means of serial IVUS and Doppler studies.

Methods: Two groups (Gr.) of patients (P) were studied sequentially: Gr. I (20 P) immediately (<3 months) and 12 months after heart transplantation (Htx). Gr. II (26 P) late (>12 months, mean 79 ± 26) after Htx and 12 months thereafter. Baseline and hyperemic coronary flow average peak velocity were measured to calculate CFR (16 µg adenosine, 0.014 in. Doppler guide wire). IVUS was performed to determine the mean plaque index (PI = [vessel area − lumen area] × 100/vessel area) of the vessel studied with Doppler. The use of a motorized IVUS pull-back system in all 92 studies allowed the identification of corresponding sites between baseline (BaseL) and follow-up (F-up) study.

Results:

	PI (%)		ΔPI (%)	CFR		ΔCFR
	BaseL	F-up		BaseL	F-up	
Gr. I	7 ± 10	17 ± 12*	10 ± 10	2.6 ± 0.7	3.4 ± 0.9*	0.8 ± 0.8
Gr. II	16 ± 13	22 ± 13¶	5 ± 11	3.4 ± 0.8	3.5 ± 0.9	0.1 ± 0.7

(*= p < 0.001, ¶ = p < 0.02 F-up vs. BaseL)

Conclusion: Despite a marked progression of TxCAD in the first year after transplantation, an improvement of CFR to high normal values was observed. Late after Htx, CFR remained unchanged, although intimal hyperplasia further increased. Thus, endothelial independent CRF is not a reliable functional parameter to assess the progression of TxCAD in the first year and late after Htx.

2:30

853-3 Ultrasound Evidence of Comparable Lesion Severity at Proximal and Distal Sites in Transplant Coronary Disease

S.R. Kapadia, E.M. Tuzcu, T.D. Crowe, K.M. Ziada, J.B. Young, C. Bott-Silverman, C. Narins, S.E. Nissen. *The Cleveland Clinic Foundation, Cleveland, Ohio, USA*

Background: Necropsy studies of transplant coronary disease suggest more severe disease occurs in distal vessels, but post-mortem examination rarely encounters patients soon after transplantation.

Methods: Intravascular ultrasound was performed in 93 patients, 1 month and 1 year after transplantation (mean 27 ± 15 and 370 ± 24 days). Arteries were divided into proximal and distal segments using the Coronary Artery Surgery Study (CASS) classification. Matched sites at baseline and follow-up examinations were analyzed for maximal intimal thickness (Pmax). A lesion (Pmax >0.5 mm) present at baseline was defined as a donor lesion and a lesion identified on follow-up at a previously normal site was defined as a de novo lesion.

Results: Of 617 sites studied at 1 year, 89 had donor and 107 had de novo lesions. Pmax for both donor and de novo lesions was similar in proximal